PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

ULTRA-TECHNEKOW™ V4

Sodium Pertechnetate Tc 99m Injection

Solution for Intravenous Injection, 1 to 19 Ci per generator

Diagnostic Radiopharmaceutical, V09FX01

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RECENT MAJOR LABEL CHANGES

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Sections or subsections that are not applicable at the time of authorization are not listed .

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

ULTRA-TECHNEKOW™ V4 (Sodium Pertechnetate Tc 99m Injection) is a source of sodium pertechnetate Tc 99m for use in the preparation of approved diagnostic radiopharmaceuticals, as described in the labeling of these diagnostic radiopharmaceutical kits or administered directly *in vivo*. When administered directly, sodium pertechnetate Tc 99m is indicated for:

Use in adults for:

- Thyroid Imaging;
- Salivary Gland Imaging;
- Urinary Bladder Imaging (direct isotopic cystography) for detection of vesico-ureteral reflux;
- Nasolacrimal Drainage System Imaging (dacryoscintigraphy).

Use in pediatric patients for:

- Thyroid Imaging;
- Urinary Bladder Imaging (direct isotopic cystography) for the detection of vesico-ureteral reflux.

1.1 Pediatrics

Pediatrics (< 18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Ultra-Technekow V4 in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use (see Section 1 INDICATIONS).

1.2 Geriatrics

Geriatrics (> 65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is not associated with differences in safety or effectiveness.

2 CONTRAINDICATIONS

Sodium pertechnetate Tc 99m Injection is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see Section 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions
Radiopharmaceuticals should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Sodium pertechnetate Tc 99m is administered by intravenous injection. When imaging the nasolacrimal drainage system, instill the sodium pertechnetate Tc 99m by the use of a device such as a micropipette or similar method which will ensure the accuracy of the dose.

For imaging the urinary bladder and ureters (direct isotopic cystography), the sodium pertechnetate Tc 99m is administered by direct instillation aseptically into the bladder via a urethral catheter, following which the catheter is flushed with approximately 200 mL of sterile saline directly into the bladder.

4.2 Recommended Dose and Dosage Adjustment

The suggested dose ranges for the average adult patient (70 kg) based on diagnostic indications are:

Indications in adult patients	**Suggested dose ranges (MBq)**
Vesico-ureteral imaging	18.5 to 37 (0.5 to 1 mCi)
Thyroid gland imaging	37 to 370 (1 to 10 mCi)
Salivary gland imaging	37 to 185 (1 to 5 mCi)
Nasolacrimal drainage system	Maximum dose of 3.7 (100 µCi)

The suggested dose ranges for pediatric patients based on diagnostic indications are:

Indications for pediatric patients	**Suggested dose ranges (MBq)**
Vesico-ureteral imaging	18.5 to 37 (0.5 to 1 mCi)
Thyroid gland imaging	2.22 to 2.96 (60 to 80 µCi) per kg body weight

4.3 Reconstitution

No reconstitution is required.

Parenteral Products:

If the eluate is used to reconstitute a radiopharmaceutical kit, the radiolabeled kit should not be used after 12 hours from the time of generator elution or after the expiration time stated on the labeling for the reconstituted product, whichever is earlier. Please refer to the kit product insert for how to reconstitute the product.

4.4 Administration

The patient dose should be measured by a suitable radioactive dose calibration system prior to administration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. If the solution is discolored, discontinue use of the generator immediately. The solution to be administered as the patient dose should be clear, colourless, and contain no particulate matter.

4.5 Missed Dose

Not applicable.

4.6 Image Acquisition and Interpretation

Please refer to the monograph of the product with which it is reconstituted.

4.7 Instructions for Preparation and Use

The components of the reaction vial are sterile and non-pyrogenic. It is essential that the user follows the directions carefully and adheres to strict aseptic technique.

Use aseptic technique and wear waterproof gloves throughout the entire preparation procedure.

Make all transfers of radioactive solutions with an adequately shielded syringe and maintain adequate shielding around the vial during the useful life of the radioactive product.

1. Immediately upon delivery, the generator should be placed within a minimum of one inch (2.54 cm) of lead shielding in such a manner so as to minimize radiation exposure to attending personnel.
2. Use a shielded syringe to withdraw patient dose or to transfer sodium pertechnetate Tc 99m into mixing vials during kit reconstitution and maintain adequate shielding during the useful life of the radioactive product.
3. The needles in the generator are sterile beneath their covers, and the generator has been cleaned underneath the top cover. Additional disinfection of these areas with agents containing alcohol may unfavorably influence the technetium Tc 99m yield.
4. Eluting the generator every 24 hours will provide optimal amounts of sodium pertechnetate Tc 99m. However, the generator may be eluted whenever sufficient amounts of technetium Tc 99m have accumulated within the column. For example:

Time After First Elution (hrs.)	Approximate Yield (% of First Elution)
1	10
2	19
3	27
4	35
5	41
6	47

Elution

1) Lift the generator by its handle and place it inside the auxiliary shield. Move the handle so that it is not covering the generator top by pushing it off to the side in between the generator and the auxiliary shield.
2) Remove and store the elution hood cover. Place the auxiliary shield top onto the top of the generator and align it with the elution hood.
3) Using forceps, remove the tip cap plugs from the needles by pulling straight up and then store for later replacement prior to generator return.
4) Remove the flip-top cap of the eluant vial; disinfect the stopper with a bactericide such as 70% isopropyl alcohol, allowing the stopper to dry before use. Invert the eluant vial and place stopper first into the saline vial alignment insert. Place the saline vial alignment insert and vial into the saline port of the auxiliary shield top and firmly push down the eluant vial until it is punctured and seated at the base of the eluant needles.
5) Place the saline shield on top of the auxiliary shield top to cover the eluant vial.
6) Remove the flip-top cap of an evacuated vial; disinfect the stopper, allowing the stopper to dry before use. Place the evacuated vial into the elution tool.
7) Position the shielded evacuated vial by carefully lowering the elution tool into place on the elution needle. Piercing the septum of the evacuated vial with the elution needle will begin the elution process.
8) Wait until the evacuated vial has completely filled itself. This may take a few minutes. **Never interrupt the elution by lifting the elution tool.**
   NOTE: Do not use generator eluate if its appearance is discoloured and discontinue use of the generator.
9) Remove the flip-top cap of the Technestat™ vial; disinfect the stopper, allowing the stopper to dry before use. Secure the Technestat vial into the Technestat vial holder.
10) Carefully remove the elution tool and replace with the shielded Technestat vial.
11) Perform a quality control verification on the eluate as per Directions for Quality Control (see below).

Subsequent Elutions

1) Remove the saline shield and then remove the saline vial alignment insert from the saline port to remove the eluant vial from the eluant needles. Remove the vial from the saline vial alignment insert and reuse the saline vial alignment insert for subsequent

elutions.

2) Remove the shielded Technestat vial by carefully lifting the Technestat vial shield from the elution needle.
3) Repeat steps 4 through 12 of the Elution procedure.

Vacuum Loss

If the vacuum in the collecting vial is lost, do not attempt to re-evacuate the vial but discard and use a new collecting vial.

Directions for Quality Control
The following quality controls steps should be performed with the eluate following each elution of Ultra-Technekow V4 Generator:

1. Determine the technetium Tc 99m concentration and molybdenum Mo 99 content for dispensing purposes. The generator eluate may be assayed using an ionization chamber dose calibrator, scintillation detector or other appropriate detection system. The manufacturer's instructions for operation of the instrument/equipment should be followed for measurement of technetium Tc 99m and molybdenum Mo 99 activity.

   NOTE**:** the acceptable molybdenum Mo 99 breakthrough limit is 0.15 kilobecquerel molybdenum Mo 99 per megabecquerel technetium Tc 99m (0.15 microcurie molybdenum Mo 99 per millicurie technetium Tc 99m) per administered dose, at the time of administration (see USP, Sodium Pertechnetate Tc 99m Injection).

2. Determine the aluminum ion concentration of the eluate.

   NOTE**:** the acceptable aluminum ion breakthrough limit is no more than 10 micrograms per milliliter of eluate (see USP, Sodium Pertechnetate Tc 99m Injection).

3. Determine the radiochemical purity of the eluate.

   NOTE: the radioactivity of the pertechnetate band is not less than 95% of the total radioactivity in the test specimen (see USP, Sodium Pertechnetate Tc 99m Injection).

4.8 Radiation Dosimetry

The estimated absorbed radiation doses from an intravenous injection of various doses of sodium pertechnetate Tc 99m distributed uniformly in the total body of an average adult and pediatric patient are shown in Table 1 and 2, respectively (per *International Commission on Radiological Protection* (ICRP) 30 and 80).

Table 1: Adult Absorbed Radiation Doses (mGy) from Intravenous Injection.

ORGAN	Absorbed Radiation Dose (mGy) for a 1110 MBq (30 mCi) Dose	rad/mCi
Adrenals	4.1	0.41
Brain	2.2	0.22
Breasts	2	0.2
Gallbladder Wall	8.3	0.83
LLI Wall	23	2.3
Small Intestine	18	1.8
Stomach	29	2.9
ULI Wall	63	6.3
Heart Wall	3.5	0.35
Kidneys	6	0.6
Liver	4.7	0.47
Lungs	2.9	0.29
Muscle	3.6	0.36
Ovaries	11	1.1
Pancreas	6.3	0.63
Red Marrow	4.1	0.41
Bone Surfaces	6.2	0.62
Skin	2	0.2
Spleen	4.8	0.48
Testes	3.1	0.31
Thymus	2.7	0.27
Thyroid	24	2.4
Urinary Bladder	20	2.0
Uterus	9	0.9
Remaining Tissues	3.9	0.39

Effective Dose Equivalent (mSv/MBq) (rem/mCi): Not available

Effective Dose (mSv/MBq) (rem/mCi) : 14

Table 2: Pediatric Absorbed Radiation Doses (mGy) from Intravenous Injection.

Age	**15 years**	**10 years**	**5 years**	**1 year**
Administered activity in MBq (mCi)	**1110 (30)**	**740 (20)**	**555 (15)**	**370 (10)**
Organ				
Adrenals	5.3	5.4	6.2	7.1
Urinary Bladder Wall	26	22	18	22
Bone Surfaces	7.6	7.5	8.1	10
Brain	2.8	3.1	3.7	4.5
Breasts	2.6	2.6	3.2	4.1
Gallbladder Wall	11	12	13	13

Stomach Wall	38	36	43	59
Small Intestine	22	23	26	30
ULI Wall	81	89	110	140
LLI Wall	31	33	40	48
Heart Wall	4.5	4.6	5.2	6.4
Kidneys	7.2	6.9	7.8	8.5
Liver	6	6.7	8	9.1
Lungs	3.8	3.8	4.4	5.3
Muscle	4.5	4.5	5	6
Muscle	4.5	4.5	5	6
Ovaries	14	13	14	17
Pancreas	8.1	8.2	8.9	10
Red Marrow	5.1	5	5.2	6
Skin	2.5	2.6	3.2	3.8
Spleen	6	6	6.7	7.8
Testes	4.1	4.3	4.9	6
Thymus	3.6	3.5	4.2	5.3
Thyroid	40	41	67	81
Uterus	11	11	12	14
Remaining Tissues	4.8	4.8	5.4	6.4
Effective Dose (mSv)*	***19***	***19***	***23***	***29***

*To obtain radiation absorbed dose in rads (30 mCi dose) from the above table, divide individual organ values by a factor of 10 (does not apply for effective dose).

The estimated absorbed radiation doses to an adult patient from the nasolacrimal imaging procedure using a maximum dose of 3.7 MBq (100 µCi) of Sodium pertechnetate Tc 99m are shown in Table 3.

Table 3: Adult Absorbed Radiation Doses from Dacryoscintigraphy
(MIRD Dose Estimate Report No. 8, *J. Nucl. Med*., 17:74-77, 1976).

	3.7 MBq (100 µCi) Dose of sodium pertechnetate Tc 99m	
Tissue	**mGy**	**rad**
Eye (Lens): If lacrimal fluid turnover is 16%/min	0.140	0.014
If lacrimal fluid turnover is 100%/min	0.022	0.002
If drainage system is blocked	4.020	0.402
Total Body *	0.011	0.001
Ovaries*	0.030	0.003
Testes*	0.009	0.001
Thyroid*	0.130	0.013

* Assuming no blockage of draining system.

In pediatric patients, an average 30-minute exposure to 37 MBq (1 mCi) of Tc 99m pertechnetate following instillation for direct cystography will result in the following estimated radiation doses.

Table 4: Pediatric Absorbed Radiation Doses from Cystography

(*International Commission on Radiological Protection (ICRP)* 30 & 80).

Age	Bladder wall dose mGy (rad)	Gonadal dose mGy (rad)
1 year	3.6 (0.36)	0.15 (0.015)
5 years	2.0 (0.2)	0.095 (0.0095)
10 years	1.3 (0.13)	0.066 (0.0066)
15 years	0.92 (0.092)	0.046 (0.0046)

5 OVERDOSAGE

In the event of a radiation overdose, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body using reinforced hydration and frequent bladder voiding. A diuretic might also be considered. If possible, an estimate of the radioactive dose given to the patient should be performed. For management of a suspected drug overdose, contact your regional poison control center.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Ultra-Technekow V4 (technetium Tc 99m) is a generator that is available in the following activities of molybdenum Mo 99 at the date and time of calibration stated on the label.

Table 5: Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition		Non-medicinal Ingredients
Intravenous or direct administration by drainage	Activity of Molybdenum Mo 99		Sodium chloride, water.
Catalog #	**GBq**	**Curie**	
N9010	37	1	
N9015	55.5	1.5	
N9020	74	2.0	
N9025	92.5	2.5	
N9030	111	3.0	
N9035	129.5	3.5	
N9051	185	5.0	
N9060	222	6.0	
N9075	227.5	7.5	
N9110	407	11.0	
N9140	518	14.0	
N9160	592	16.0	
N9190	703	19.0	

Each generator is supplied with the following components for the elution of the generator:

1 - Technestat Vial (5 mL) containing 0.5 mL of 1.5 mg/mL methylparaben and 0.2 mg/mL propylparaben, sterile, non-pyrogenic

1 - Package Insert

Supplied Separately:

30 - Evacuated Collecting Vials (30 mL), sterile, non-pyrogenic, supplied with:
90 - Radioactive Materials Labels – Collection Vial (30 en, 30 fr, 30 es)
90 - Radioactive Materials Labels – Elution Shield (30 en, 30 fr, 30 es)
1 - Package Insert
30 - Generator Eluant, 0.9% Sodium chloride, sterile, non-pyrogenic, available in 5, 10, or 20 mL volumes, with 1 package insert. The eluant does not contain an antimicrobial agent.

6.1 Physical Characteristics

Technetium Tc 99m decays by isomeric transition with a physical half-life of 6 hours (Stabin MG, da Luz CQPL. Decay Data For Internal and External Dose Assessment, *Health Phys.* 83(4):471-475, 2002). The principal photon that is useful for detection and imaging studies is listed in Table 6.

Table 6: Principal Radiation Emission Data.

Radiation	Mean % per Disintegration	Energy (keV)
Gamma-2	89.07	140.5

Molybdenum Mo 99 decays to technetium Tc 99m with a molybdenum Mo 99 half-life of 2.75 days or 66 hours. The physical decay characteristics of molybdenum Mo 99 are such that only 88.6 % of the decaying molybdenum Mo 99 atoms form technetium Tc 99m. Generator elutions may be made at any time, but the amount of technetium Tc 99m available will depend on the interval measured from the last elution. Approximately 47% of the maximum available technetium Tc 99m is reached after 6 hours and 95% after 23 hours. To correct for physical decay of molybdenum Mo 99 and technetium Tc 99m, the fractions that remain at selected intervals of time are shown in Table 7 and 8 (data from Stabin MG, da Luz CQPL. Decay Data For Internal and External Dose Assessment, *Health Phys*. 83(4):471-475, 2002). Table 9 shows the principal photons that are useful for detection and imaging studies (Kocker, David C., "Radioactive Decay Tables," DOE/TIC-11026, p. 108, (1981)).

Table 7: Physical Decay Chart, Molybdenum Mo99, Half-Life 66 hours.

Days	Percent Remaining	Days	Percent Remaining
0	100	10	8
1	78	11	6
2	60	12	5
3	47	13	4
4	37	14	3
5	28	15	2
6	22	20	0.6
7	17	25	0.2
8	13	30	0.05
9	10		

Table 8: Physical Decay Chart, Technetium Tc99m, Half-Life 6 hours.

Hours	Percent Remaining	Hours	Percent Remaining
0*	100	9	36
1	89	10	32
2	79	11	28
3	71	12	25
4	63	14	20
5	56	16	16
6	50	18	13
7	45	24	6
8	40		

*at calibration time.

Table 9: Principal Radiation Emission Data for Mo-99.

Radiation	Mean % per Disintegration	Energy (keV)
Gamma-3	3.8	140.5
Gamma-6	6.2	181.1
Gamma-21	12.8	739.6
Gamma-23	4.5	778.0
Beta-3	17.3	436.0 (max)/133.0 (ave)
Beta-5	82.7	1214.0 (max)/442.7(ave)

6.2 External Radiation

The specific gamma ray constant for technetium Tc 99m is 0.795 R/hr-mCi at 1 cm. The first half-value layer is 0.023 cm of lead (Pb). A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of lead (Pb) is shown in Table 10. For example, the use of 0.27cm thickness of lead (Pb) will

attenuate the radiation emitted by a factor of about 1000 (Smith David S.; Stabin, Michael G. Exposure Rate Constants and Lead Shielding Values for Over 1,100 Radionuclides, *Health Physics*. 102(3):271-291, March 2012).

Table 10: Radiation Attenuation by Lead Shielding.

Shield Thickness (Pb, cm)	Coefficient of Attenuation
0.023	0.5
0.09	0.1
0.18	0.01
0.27	0.001

7 WARNINGS AND PRECAUTIONS

Please see Section 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

Radiopharmaceuticals should be administered under the supervision of a health professional who is qualified by training and experience in the safe use of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

The radiopharmaceutical product may be received, used and administered only by authorized persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of local competent official organizations.

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers, members of the patient's household, the public, and the environment.

Generally, the Tc 99m labelling reactions involved depend on maintaining the tin (stannous ion) in the reduced state. Hence, sodium pertechnetate Tc 99m containing oxidants should not be employed.

General

Only use generator eluant specified for use with the Ultra-Technekow V4 Generator. Do not use any other generator eluant or saline from any other source.

Carcinogenesis and Mutagenesis

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential. However, long-term cumulative radiation exposure may be associated with an increased risk of cancer.

Contamination

The following measures should be taken for up to 12 hours after receiving the radiopharmaceutical product:

- Toilet should be used instead of urinal.
- Toilet should be flushed several times after use.

Special precautions such as bladder catheterization should be taken following administration to incontinent patients to minimize the risk of radioactive contamination of clothing, bed linen and the patient's environment.

If blood or urine gets onto clothing such clothing should be washed separately or stored for 1-2 weeks to allow for decay.

Ear/Nose/Throat

Following the nasolacrimal imaging procedure, to further minimize the radiation dose, the nose should be flushed with sterile distilled water or an isotonic sodium chloride solution and blown.

Ophthalmologic

Following the nasolacrimal imaging procedure, to further minimize the radiation dose, eyes should be washed with sterile distilled water or an isotonic sodium chloride solution.

Reproductive Health: Female and Male Potential

- **Fertility**

No long-term animal studies have been performed to evaluate whether sodium pertechnetate Tc 99m affects fertility in males or females.

7.1 Special Populations

7.1.1 Pregnant Women

In animal reproductive studies (Gilbert et al, 1996. Owunwanne et al, 1998. Wegst et al, 1983), sodium pertechnetate Tc 99m (as free pertechnetate) has been shown to cross the placental barrier. It is not known whether sodium pertechnetate Tc 99m can cause fetal harm when administered to a pregnant woman or affect reproductive capacity.

Ideally examinations using radiopharmaceuticals, especially those elective in nature of women of childbearing capability, should be performed during the first ten days following the onset of menses, or after ensuring the woman is not pregnant. The benefit of using a diagnostic radiopharmaceutical should be weighed against the possible risk to an embryo or a fetus.

7.1.2 Breastfeeding

Technetium Tc 99m is excreted in human milk during lactation. Where an assessment of the risk to benefit ratio suggests the use of this product in nursing women, formula-feeding should be substituted for breastfeeding for at least 12 hours after administration of sodium pertechnetate Tc 99m and feeds expressed during this period should be discarded.

7.1.3 Pediatrics

Radiation risks associated with the use of sodium pertechnetate Tc 99m are greater in pediatric

patients than in adults owing to greater absorbed radiation doses and longer life expectancy. These greater risks should be taken firmly into account in all benefit risk assessments involving pediatric patients.

7.1.4 Geriatrics

There is no evidence to suggest that use in the geriatric population is associated with differences in the safety or effectiveness of this product.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Allergic reactions including anaphylaxis have been reported infrequently following the administration of sodium pertechnetate Tc 99m.

Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container should advise their physician. For a complete listing, see Section 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

8.2 Clinical Trial Adverse Reactions

No data available.

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

No data available.

8.3 Less Common Clinical Trial Adverse Reactions

No data available.

8.3.1 Less Common Clinical Trial Adverse Reactions – Pediatrics

No data available.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings: No data available.

Post-Market Findings: No data available.

8.5 Post-Market Adverse Reactions

No data available.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No data available.

9.3 Drug-Behavioural Interactions

No data available.

9.4 Drug-Drug Interactions

Interaction with other drugs have not been established.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

The pertechnetate ion distributes throughout the body similarly to the iodide ion but is not organified when trapped in the thyroid gland. The pertechnetate ion concentrates within the thyroid gland, salivary glands, stomach and choroid plexus, and gradually equilibrates within the extracellular space. A fraction of pertechnetate ion is promptly excreted via the kidneys.

Following the administration of sodium pertechnetate Tc 99m as an eye drop, the drug mixes with tears within the conjunctival space. Within seconds to minutes it leaves the conjunctival space and escapes into the inferior meatus of the nose through the nasolacrimal drainage system. During this process, the pertechnetate ion passes through the canaliculi, the lacrimal sac and the nasolacrimal duct. In the event of any anatomical or functional blockage of the drainage system there will be a backflow resulting in tearing (epiphora). Thus, the pertechnetate escapes the conjunctival space in the tears.

10.2 Pharmacodynamics

No data available.

10.3 Pharmacokinetics

No data available.

Absorption: No data available.

Distribution: No data available.

Metabolism: No data available.

Elimination: While the majority of pertechnetate escapes within a few minutes of normal drainage and tearing, it has been documented that there is some degree of transconjunctival absorption with a turnover of 1.5% per minute in normal individuals, 2.1% per minute in patients without any sac and 2.7% per minute in patients with inflamed conjunctiva due to chronic dacryocystitis. Individual values may vary but these rates are representative and indicate that the maximum possible pertechnetate absorbed will remain below one thousandth of that used in other routine diagnostic procedures.

Duration of Effect: Not applicable.

Special Populations and Conditions: No data available.

11 STORAGE, STABILITY AND DISPOSAL

Keep the generator in its plastic container and store between 20° to 25°C (68° to 77°F). Keep the eluted sodium pertechnetate solution in adequate shielding and store between 20° to 25°C (68° to 77°F).

The generator should not be used after the expiration date stated on the label.

Once eluted from the generator, sodium pertechnetate Tc 99m solution is considered expired after 12 hours. If the eluate is used to reconstitute a radiopharmaceutical kit, the radiolabeled kit should not be used after 12 hours from the time of generator elution or after the expiration time stated on the labeling for the reconstituted product, whichever is earlier.

Return the expired generator to Curium US LLC or dispose in accordance with applicable regulations.

12 SPECIAL HANDLING INSTRUCTIONS

As with any other radioactive material, care should be taken to minimize radiation exposure to the patient and to ensure minimal radiation exposure to occupational workers.

Expired Generator Disposal:

1. Following the life of the generator, remove and dispose of the used Technestat vial and the eluant vial.
2. Cover the elution and eluant needles with the stored tip cap plugs using tip cap placement tool.
3. Place the stored elution hood cover onto the top of the generator.
4. The intact generator assembly should be returned to Curium US LLC (1-866-855-5988) or disposed of in accordance with applicable regulations.

Potential radioactive components or remaining product should be, whenever possible, safely stored for decay until they meet unconditional clearance levels per SOR/2000-207 as prescribed by Canada Nuclear Safety Commission. When unconditional clearance levels cannot be achieved, the radioactive waste should be disposed of as per the Canadian Nuclear Safety Commission and/or other applicable authority.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

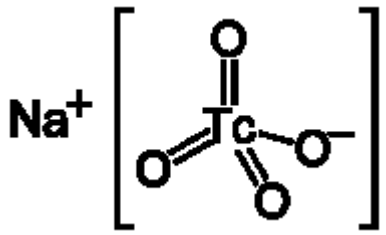
Drug Substance

Proper name: Sodium pertechnetate Tc 99m.

Chemical name: Sodium pertechnetate Tc 99m.

Molecular formula and molecular mass: $NaTcO_4$, 169.89 g/mol.

Structural formula:



Physicochemical properties:

The physical decay of molybdenum Mo 99 adsorbed onto the column of the generator produces technetium Tc 99m which is then eluted using a 0.9% Sodium chloride solution that is sterile and non-pyrogenic.

Sodium pertechnetate (Tc 99m) is eluted from the generator as a clear, colourless, sterile, non-pyrogenic isotonic solution free from visible foreign matter and antimicrobial agents.

Sodium pertechnetate solution has a pH of 4.5 – 7.5 and contains at least 95% of the (Tc 99m) activity as pertechnetate (TcO_4).

Sodium pertechnetate solution should not contain more than the USP limit of 0.15 kilobecquerel molybdenum Mo 99 per megabecquerel technetium Tc 99m (0.15 microcurie molybdenum Mo 99 per millicurie technetium Tc 99m) per administered dose at the time of administration and an aluminum ion concentration of no more than 10 micrograms per milliliter of the generator eluate, both of which must be determined by the user before administration. See Directions for Quality Control in Section 4.7 Instructions for preparation and use.

Since the eluate does not contain an antimicrobial agent, it should not be used after 12 hours from the time of elution.

Tc 99m decay produces an emission of gamma radiation useful for detection and imaging studies. The half-life of Tc 99m is 6 hours and the energy of the principal photon emitted is

140.5 keV (89.07%). The eluate collection vial should be kept in a radiation shield. See Section 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING for the Tc 99m decay table and external radiation attenuation.

Product Characteristics:

Ultra-Technekow V4 (technetium Tc 99m generator) consists of a column containing fission produced molybdenum Mo 99 adsorbed on alumina. The column is enclosed in a lead or depleted uranium shield. The column assembly and shielding are encased in a plastic container that is covered with a plastic elution hood. The elution hood has an opening for the column assembly double inlet needles and an opening for the single outlet needle. The needles accommodate the sterile eluant vials and sterile evacuated collection vials. A sterile 0.22 micrometer bacteriological filter is incorporated between the column outlet and the collection vials. The eluting solvent consists of a 0.9% sodium chloride solution that is sterile and non-pyrogenic.

A sterile vial containing a bacteriostatic agent is supplied with the generator and should be used to aseptically seal the collect needle after each elution.

The generator is provided as a closed system for the production of a sterile metastable solution of technetium Tc 99m in 0.9% sodium chloride. Tc 99m is produced by the decay of molybdenum Mo 99. See Section 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING for the molybdenum Mo 99m decay table and external radiation attenuation.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

No data available.

14.2 Study Results

No data available.

14.3 Comparative Bioavailability Studies

No data available.

14.4 Immunogenicity

No data available.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether Sodium Pertechnetate Tc 99m Injection affects fertility in males or females. As with other radiopharmaceuticals which distribute intracellularly, there may be increased risk of chromosome damage from Auger electrons if nuclear uptake occurs.

Carcinogenicity: Not available.

Genotoxicity: Not available.

Reproductive and Developmental Toxicology: Not available.

Special Toxicology: Not available.

Juvenile Toxicity: Not available.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

ULTRA-TECHNEKOW™ V4

Sodium Pertechnetate Tc 99m Injection

Read this carefully before you receive your exam using **Sodium Pertechnetate Tc 99m Injection**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Ultra-Technekow V4**.

Serious Warnings and Precautions

Ultra-Technekow V4 is a radiopharmaceutical. It can only be used under the supervision of physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

What is Ultra-Technekow V4 used for?

- Ultra-Technekow V4 will always be used in a hospital or healthcare setting. It will only be administered to you by a qualified health care professional trained to safely handle radioactive material. Your doctor will decide the sodium pertechnetate Tc 99m solution amount to be used. The dose administered will depend on the procedure.
- The Ultra-Technekow V4 generator is a source of sodium pertechnetate Tc 99m that can be used directly or with radiopharmaceutical kits to prepare medications to help your doctor make a diagnosis.
- Sodium pertechnetate Tc 99m is used in adults and children to image the thyroid and urinary bladder.
- Sodium pertechnetate Tc 99m is also used in adults to image the salivary glands and tear ducts.

How does Ultra-Technekow V4 work?

Ultra-Technekow V4 generator consists of radioactive Molybdenum Mo 99 absorbed to a non-radioactive column. Molybdenum Mo 99 decays to become Tc 99m. Rinsing the column with a saline solution separates out the Tc 99m to produce a radioactive solution called sodium pertechnetate Tc 99m. Sodium pertechnetate Tc 99m is a radioactive tracer. When administered into the body, it collects in certain organs. The areas where radioactivity is deposited can be imaged from outside the body using special cameras which capture an image called a scan. Scans show the distribution of radioactivity within the organs of the body and help doctors make a diagnosis.

What are the ingredients in Ultra-Technekow V4?

Medicinal ingredients: Sodium pertechnetate Tc 99m.

Non-medicinal ingredients: Sodium chloride, water.

Ultra-Technekow V4 comes in the following dosage forms:

Generator between 1 to 19 curies.

Do not use Ultra-Technekow V4, Sodium Pertechnetate Tc 99m Injection if:

- You are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredients, or component of the container.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you receive Ultra-Technekow V4, Sodium Pertechnetate Tc 99m Injection. Talk about any health conditions or problems you may have, including if:

- You have had an allergic reaction to this radiopharmaceutical or its ingredients in the past.
- You might be pregnant. If there is a need to consider the use of Ultra-Technekow V4, Sodium Pertechnetate Tc 99m Injection during pregnancy, your doctor will discuss the benefits and risks with you.
- You are breastfeeding. Technetium Tc 99m is excreted in human milk during lactation; therefore formula-feeding should be substituted for breastfeeding for at least 12 hours after administration of sodium pertechnetate Tc 99m and feeds expressed during this period should be discarded.

Other warnings you should know about:

The following safety precautions should be followed for up to 12 hours after receiving sodium pertechnetate Tc 99m:

- Men should use toilet instead of urinal.
- Toilet should be flushed several times after use.
- Wash hands thoroughly after using the toilet.
- Clothing contaminated with urine or blood should be washed separately or stored for 1-2 weeks to allow for decay.
- Blow your nose and wash your eyes with sterile distilled water after tear ducts imaging procedure.
- Special precautions such as bladder catheterization should be taken following administration to incontinent patients to minimize the risk of radioactive contamination of clothing, bed linen and the patient's environment.

Also:

- Radiation risks may be greater in children and younger people compared to people who

are older.
- Exposure to radiation for long periods of time throughout a person's life may increase the risk of cancer.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Sodium Pertechnetate Tc 99m Injection eluted from Ultra-Technekow V4:

No known interactions with this drug have been documented; however, your doctor should be informed about all the prescribed or over-the-counter products you use.

How to take Ultra-Technekow V4, Sodium Pertechnetate Tc 99m Injection:

This product is not self-administered. Ultra-Technekow V4, Sodium pertechnetate Tc 99m solution, will be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals.

Usual dose:

Your healthcare professional will decide on the dose that is right for you. The dose depends on your exam and on the product with which it is radiolabelled, if any.

Overdose:

If you think you, or a person you are caring for, have received too much sodium pertechnetate Tc 99m, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

Not applicable.

What are possible side effects from using Ultra-Technekow V4, Sodium Pertechnetate Tc 99m Injection?

These are not all the possible side effects you may have when receiving sodium pertechnetate Tc 99m eluted from Ultra-Technekow V4. If you experience any side effects not listed here, tell your healthcare professional.

Infrequently, a severe allergic reaction (anaphylaxis) may occur with this drug. Should you experience any side effect following the administration of Ultra-Technekow V4, Sodium Pertechnetate Tc 99m Injection, be sure to tell your doctor.

If you have a troublesome symptom or side effect that is not listed here that interferes with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Ultra-Technekow V4 and the sodium pertechnetate solution is stored in adequate shielding between 20° to 25°C. The solution should not be used after 12 hours from the time of elution.

If you want more information about Ultra-Technekow V4:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; or by calling 1-800-885-5988.

This leaflet was prepared by Curium Canada Inc.

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